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Dear Dr. Heidelberger:

I am engaged in writing a book on immunology. That means, of course, that there will be a chapter on antibody-antigen reactions. And that means of course that I must discuss the lattice theory, so ably championed by yourself, among others (including Pauling).

It is my wish to be as fair as possible in this discussion (though I do not say I shall not be polemical). Therefore it is quite important for me to understand your point of view as fully as I can. I am therefore sending to you copies of a number of statements made, not by Hooker or myself, but by another well known scientist, whose name I do not feel justified in using, which state his opinion of the relative places of the lattice theory and the older Bordet theory. I should like to ask of you your opinion of each statement, whether you agree with it, and in case you do not, a brief statement (or reference to a page of your writings) where such reasons are offered) of your reasons for ~~not~~ disagreeing with the statement. If you are willing to do this it will be of considerable assistance to me, although you of course realize that anything you say to Hooker and Boyd is likely to be used against you.

When my chapter on antibody-^t antigen reactions has been revised into a presentable state, I should like to ask you to read it, if you would be willing to spare the time. That would enable you to protest against any (unconsciously, I assure you) unfair treatment of your opinions.

Hooker and I look forward to seeing you this spring at the symposium on immunochemistry before the N.Y. Acad. Sci., which you so kindly invited us to. We are carrying out some quantitative studies on horse-anti-hemocyanin which I feel will be worth reporting. (Also some experiments designed to test the lattice theory).

Sincerely,

William C. Boyd

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a. I think it is generally agreed that the agglutination reaction consists of two steps; one, combination of antibody with bacteria and, two, agglutination of the sensitized suspension. The combination between antibody and bacteria is, I think, correctly accounted for by the Marrack-Heidelberger lattice theory.

b. The agglutination of the sensitized cells is, I believe, accounted for by a combination of an electrostatic repulsion and cohesive force. I do not believe the lattice theory has any bearing on this stage whatever. There are a number of experimental facts which confirm this statement of which I believe the following two are the most important.

1. As Bordet and others, including Northrop- and deKruif have shown the combination between antigen and antibody can be completely separated from agglutination by causing the combination to take place in the absence of salt. This step fits in with the lattice theory. The agglutination of this sensitized suspension upon the addition of electrolytes, can now be predicted by measurements of the electro-kinetic potential and of the cohesive force.

2. Further confirmation of the fact that the agglutination is determined by the potential is offered by the agglutination of non-sensitized bacteria and by the agglutination of bacteria with normal serum or by other proteins. All these various types of agglutination, not only of bacteria but probably of all suspensions, may be predicted by electrophoresis measurements, whereas the lattice theory can obviously apply only to specific agglutination*.

c. So far as I know the separation of specific agglutination from all the many other known agglutinations is purely arbitrary as it is extremely unlikely that an entirely different mechanism is involved in specific bacterial agglutination.

* and flocculation (W.E.B)